Serial No.: 09/622,353
Group Art Unit: 1637

REMARKS

Claims 1-21 are under examination and pending in the case. Claim 2 is amended. No new matter is introduced.

35 U.S.C. §112, 2nd Paragraph

Claim 2 was rejected under §112, 2nd paragraph as being indefinite. The Examiner stated that it is unclear whether the language "an amplification product" is referred from the amplification product from step (e) of claim 1. Claim 2 has been amended to recite proper antecedent reference to "said amplification product" of step (f). Withdrawal of the rejection is requested.

35 U.S.C. §103

Claims 1,4-7, 9-13, and 15-21 were rejected under §103(a) as being unpatentable over Briggs *et al.* (U.S. Pat. No. 5,962,764) in view of Lindemann *et al.* (U.S. Pat. No. 5,958,738). Claims 2 and 8 were rejected in further view of Schnable *et al.* (U.S. Pat. No. 5,684,242). Claims 3 and 14 were rejected in further view of Halverson *et al.* (U.S. Pat. No. 5,707,809). Applicants respectfully traverse.

A. Briggs *et al.* Requires a Gene of Known Sequence – the Claimed Invention Doesn't

The Examiner cites Briggs *et al.* as disclosing a method for determining the function of a gene involving the use of the Mutator family of transposable elements. While Briggs et al. does disclose Mutator, the method of Briggs *et al.* is entirely different from the claimed invention. In Briggs *et al.* one can determine an otherwise unknown phenotype for a gene of known sequence. In contrast, the claimed invention enables one to isolate an unknown sequence given a known phenotype. Briggs *et al.* employ primers to the transposable element and to the known genetic sequence. In the claimed invention, primers are annealed to the adapter and transposable element; primers are not annealed to the genetic sequence. The claimed invention acts to isolate the unknown genetic sequence. Indeed, if one had a gene of known sequence

as in Briggs *et al.* then the claimed invention would be unnecessary. Briggs *et al.* fails to teach how to isolate an unknown genetic sequence as does the claimed invention and does little else with respect to the claimed invention but make reference to the Mutator family of transposable elements.

B. Lindemann *et al.* is Inoperable as Modified for the Claimed Invention

The Examiner states that the primer binding sites taught by Lindemann *et al.* "suggest that the primer is nested as recited in step (e) of claim 1 and step (d) of claim 15 and the oligonucleotide of Lindemann *et al.* has the same function as the recited adapter in steps (d)-(e) of claim 1 and steps (c)-(d) of claim 15 and claim 10." (emphasis added) Page 5, 1st paragraph. The Examiner is incorrect.

Lindemann *et al.* teaches that the nested primer binding sites are contained entirely within the oligonucleotide adapters. For example, Lindemann *et al.* state that the "multiple primer binding sites contained within or encoded by an adapter may overlap one another to generate nested primer binding sites, or the primer binding sites may be discrete." (emphasis added) Column 16, lines 60-64; see also, column 14, lines 50-59. In Lindemann *et al.* amplification proceeds from a single primer that anneals only to the adapter. In contrast, in the claimed invention amplification is obtained by annealing primers to both the transposable element and to the adapter. Clearly, the primers of Lindemann *et al.* do not have the same function as the primers in claim 1 or claim 15.

Lindemann *et al.* is also cited as teaching a method for obtaining polynucleotides comprising sequences that differ between two populations of DNA. But the present invention teaches a method of identification and isolation of a genetic sequence that is present in both populations of DNA. In the claimed invention, the genomic DNA of both populations of organisms comprises at least one transposable element. In sharp contrast, in Lindemann *et al.* a nucleic acid is entirely absent in one population relative to another. The presently claimed invention is drawn to insertions that differ not with respect to their absence or presence but as to their position in the genome. Lindemann

et al. make the differential nature of their invention very clear at column 5, lines 60-64, where it states,

> The invention provides improved methods for the identification and isolation of polynucleotides comprising nucleic acid sequences present in a first (sample) cell, cell type, or cell population that are not present in one or more other (control) cell(s), cell type(s) or cell population(s). (emphasis added).

Nowhere do *Lindemann et al.* teach or suggest that their method is applicable to the populations employed in the claimed invention where transposable elements are present in both sample and control populations as recited specifically in the claimed invention. Indeed, if Lindemann *et al.* employed control and sample populations such as those employed in the claimed invention then the subtractive hybridization methodology of Lindemann *et al.* would not work for its intended function.

The Federal Circuit has stated clearly on several occasions that if a proposal for modifying the prior art in an effort to attain the claimed invention causes the art to become inoperable or destroys its intended function, then the requisite motivation to make the modification would not have existed. *In re Fritsch* 23 USPQ2d 1780, 1783 (Fed. Cir. 1992); *In re Gordon*, 221 USPQ 1125, 1127 (Fed. Cir. 1984). No motivation can be found for a modification that yields an inoperable method and, consequently, Lindemann *et al.* cannot be employed to argue for the required motivation under section 103.

In the prior response filed on April 11, 2002, the Applicants specifically requested that the Examiner detail for the record why the inoperability of Lindemann *et al.* as modified for the claimed invention fails to disqualify it as prior art. Page 8, 2nd paragraph. The Examiner has not responded to Applicants request for clarification. The Applicants again respectfully request that if the Examiner maintains this rejection that she put forth a complete response to Applicants request as required by 37 C.F.R. 1.104. See also, M.P.E.P. at §707.07.

Serial No.: 09/622,353
Group Art Unit: 1637

C. Motivation is Not Established by Mere Reference to Disparate Elements of Invention

Applicants respectfully submit that the Office Action fails to make a proper *prima facie* case of obviousness. According to the M.P.E.P. §2143, to establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.

How then does the Examiner conclude there is motivation and a reasonable expectation of success to make the claimed invention? The following logic is applied:

"The motivation is [t]hat the method of Briggs *et al.* is a rapid, inexpensive method for determining the function of a gene of known sequence involving a primer complementary to the TIP [sic] sequence of the transposable element . . . and the method of Lindemann *et al.* overcomes the disadvantage of using fewer PCR cycles, nuclease digestion before amplification and a single adapter designed for use with multiple primers." Page 6, 1st paragraph.

In this confusing paragraph, the Examiner does nothing more than make vague reference to a collection of isolated facts and elements. But it is not sufficient to simply list an assortment of disconnected facts, couple this with a statement as to motivation, and then conclude with a statement of obviousness. Instead, there must be motivation and a reasonable expectation to make the invention as claimed.

Briggs *et al.* does indeed teach rapid and inexpensive method for determining the function of a gene of known sequence. However, the present invention is not directed to determining the function of a gene of known sequence as conceded by the Examiner on page 4, 2nd paragraph of the Office action. The fact that a primer to the transposable element is employed in the method of Briggs *et al.* as well as in the claimed invention is true but adds little or nothing to support the argument of obviousness. The contention that the method of Lindemann *et al.* "overcomes the disadvantage [sic] of using fewer PCR cycles, nuclease digestion before amplification and a single adapter designed for use with multiple primers" is all well and good but how does this statement in combination with the observation made regarding the

method of Briggs *et al.* lead inexorably to a conclusion of obviousness? As stated previously as well as in the previous response, Lindemann *et al.* is a subtractive hybridization scheme that is inoperable with populations that each comprise transposable elements as in the claimed invention. What then is the legal basis for the Examiner's disregard of the inoperability of Lindemann *et al.* as modified for the claimed invention? How do a reference to Mutator and a reference to a subtractive hybridization scheme lead one to the claimed invention? Applicants find the Examiner's reasoning difficult to comprehend and request that if this rejection is maintained that a clear and logical re-statement be made of how success and motivation are established by the cited art. See, 37 C.F.R. 1.104.

D. Neither Schnable *et al.* nor Halverson *et al.* Correct the Deficiencies of Briggs *et al.* or Lindemann *et al.*

Dependent claims 2, 3, 8 and 14 were rejected as being unpatentable over Briggs et al. and Lindemann et al. in further view of Schnable *et al.* (U.S. Pat. No. 5,684,242) as applied to claims 2 and 8, and in further view of Halverson *et al.* (U.S. Pat. No. 5,707,809) as applied to claims 3 and 14. Applicants respectfully traverse.

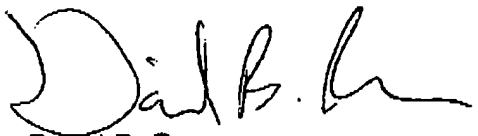
Schnable *et al.* is cited as teaching cosegregation analysis. Halverson *et al.* is cited as teaching bulked segregant analysis. But neither of the elements cited from these references can act to salvage the utter lack of incentive or reasonable expectation of success to make the claimed invention that Briggs *et al.* and Lindemann *et al.* fail to provide. Since independent claims 1 and 15 are believed to be patentable, dependent claims 2,3, 8 and 14 are also believed patentable.

Serial No.: 09/622,353
Group Art Unit: 1637

CONCLUSION

For the foregoing reasons, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §112 and §103 and passage of the application to issuance. In the event that any issues of substance remain, **APPLICANTS HEREBY REQUEST AN EXAMINER INTERVIEW PRIOR TO PREPARATION OF ANY ADDITIONAL WRITTEN ACTION BY THE EXAMINER.** Please feel free to call the undersigned to arrange for an Examiner's interview or to discuss the status of the application.

Respectfully submitted,



David B. Ran
Attorney for Applicant(s)
Registration No. 38,589

PIONEER HI-BRED INTERNATIONAL, INC.
Corporate Intellectual Property
7100 N.W. 62nd Avenue
P.O. Box 1000
Johnston, Iowa 50131-1000
Phone: (515) 334-4465
Facsimile: (515) 334-6883

Serial No.: 09/622,353
Group Art Unit: 1637

VERSION WITH MARKINGS TO SHOW CHANGES MADE

2. The method of claim 1, wherein step (f) comprises using cosegregation analysis to isolate said [an] amplification product that cosegregates with said mutant phenotype.

CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that the attached documents are being transmitted via facsimile transmission to the Assistant Commissioner for Patents of the United States Patent and Trademark Office, via facsimile number (703) 872-9306, on this 4th day of October, 2002.

David B. Ran
Attorney/Agent for Applicant
10/04/02
Date

FAX RECEIVED
OCT 07 2002
GROUP 1600

PIONEER HI-BRED INTERNATIONAL, INC.
CORPORATE INTELLECTUAL PROPERTY DEPARTMENT

OFFICIAL

FAX TRANSMISSION

7100 N.W. 62nd Avenue
P.O. Box 1000
Johnston, Iowa 50131-1000

Phone: (515) 334-4465
Fax: (515) 334-6883

TO: Assistant Commissioner for Patents

FROM: David B. Ran, Registration No. 38,589

RE: U. S. Patent Application No. 09/622,353; Attorney Docket No. 0457E-PCT-US
Title: "Transposable Element-Anchored, Amplification Method for Isolation And Identification of Tagged Genes"

DATE: October 4, 2002 FAX NUMBER: (703) 872-9306

NUMBER OF PAGE(S) FOLLOWING THIS SHEET: 8

COMMENTS:

Attached –

- **Amendment / 8 pages**